INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES
[ISSN: 0975-4725; CODEN(USA): IJPS00]
Journal Homepage: https://www.ijpsjournal.com

Review Paper

Advances in Self-Emulsifying Drug Delivery Systems: Focus on Pellet-Based Formulations

Akshay Jadhav*, Dr. Ravi Wanare, Aniket Kadam, Rehan Beniwale, Ankita Tayade

Sudhakarrao naik institute of pharmacy pusad-445204 District - yavatmal. Maharashtra. India

ARTICLE INFO

Published: 16 Apr. 2025
Keywords:
Self-emulsifying pellets, SEDDS, Extrusion-spheronization, Dissolution studies, Drug delivery system
DOI:
10.5281/zenodo.15231553

ABSTRACT

Self-emulsifying drug delivery systems (SEDDS) have emerged as a promising approach to enhance the solubility and oral bioavailability of poorly water-soluble drugs. Among these, self-emulsifying pellets represent a novel solid dosage form that combines the advantages of both SEDDS and multiparticulate systems. This review focuses on the formulation, evaluation, and optimization of self-emulsifying pellets, with particular attention to their application for delivering Venlafaxine Hydrochloride, a BCS Class I drug with high solubility and permeability. Key formulation components, including oils, surfactants, and co-surfactants, are discussed along with the role of excipients such as microcrystalline cellulose and lactose monohydrate in improving pellet properties. Various techniques employed in the preparation of pellets, including extrusion–spheronization, are critically analyzed. The review also highlights different characterization methods such as dissolution testing, droplet size analysis, and surface morphology studies that ensure product quality and performance. Optimization strategies using design of experiments (DoE) are explored for achieving desired drug release profiles. The advantages, limitations, and future prospects of self-emulsifying pellets as a drug delivery platform are also presented, emphasizing their potential for industrial scalability and patient compliance.

INTRODUCTION

These days, a growing number of medications have low and highly variable oral bioavailability due to their poor water solubility and high lipophilicity. Because of this, even though they show promise in terms of pharmacodynamic activity, many medication candidates never make it to market. However, advertised poorly water-soluble medications are administered in higher dosages than necessary to reach the desired plasma level, which increases the risk of toxicity issues. Therefore, to increase the solubility and bioavailability of poorly soluble medications,

***Corresponding Author:** Akshay Jadhav
Address: *Sudhakarrao naik institute of pharmacy pusad-445204 District - yavatmal. Maharashtra. India*
Email ✉: akshayjadhav1827@gmail.com
Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

appropriate formulation techniques must be created.[1]One of the crucial factors in achieving the required drug concentration in systemic circulation for pharmacological response is solubility, which is the phenomena of solids dissolving in liquid phases to produce homogeneous systems. After oral administration, poorly water-soluble medications may need high dosages to achieve therapeutic plasma concentrations. A drug's solubility in aqueous fluids across a range of pH values determines its bioavailability when taken orally. For poorly water-soluble substances (ISSN: 2250-1177), the oral bioavailability is limited by the drug's inadequate rate of dissolution.[2] After being diluted with gastric fluid, SEDDS, an isotropic mixture of oils, surfactant, and co-surfactant, can create oil-in-water (o/w) emulsions when gently stirred by the intestine's peristaltic movement. When passing through the GIT after oral administration, SEDDS can keep the poorly soluble medications dispersed in the tiny oil droplets.[3] The most popular methods for producing pellets in the pharmaceutical industry include pelletization technologies like extrusion/spheronization, solution-suspension layering, and powder layering. Recently, extrusion/spheronization was used to create pellets with microcrystalline cellulose and lactose combined with self-emulsifying mixes.[4] Typically made as liquids, SE formulations have some drawbacks, such as high manufacturing costs, poor stability and mobility, low drug loading, and limited dosage form options. Another issue could be the precipitation of irreversible medications or excipients. The formulations' high surfactant content (30–60%) might cause gastrointestinal (GI) irritation, which is more significant. An alternate strategy called S-SEDDS (Solid Self Emulsifying Drug Delivery System) has been researched to overcome these issues. S-SEDDS concentrate on integrating liquid or semi-solid SE components into powders or nanoparticles using a variety of solidification methods, such as melt extrusion, spray drying, adsorption to solid carriers, and nanoparticle technology. These powders or nanoparticles—which are also known as SE nanoparticles, dry emulsions, or solid dispersions—are typically formed into capsules or other solid SE dosage forms.In addition, SE capsules are those that are filled with liquid or semi-solid SEDDS without the need of a solidifying agent. S-SEDDS are a combination of SEDDS and solid dosage forms to some degree. As a result, many of their qualities (such as excipient selection, specificity, and characterisation) are the sum of the relevant properties of both solid dosage forms and SEDDS. Other solid SE dosage forms have surfaced in recent years, including SE suppositories/implants, SE microspheres/nanoparticles, and SE pellets/tablets.[5]

The benefit of SEDDS

1. Improved oral bioavailability that makes dose decrease possible.
2. Drugs are targeted selectively at a certain window of absorption in the GIT.
3. Heavy drug loading.
4. Management of delivery profiles.
5. Emulsion is a sensitive and metastable dispersed form, whereas S(M)EDDS is a formulation that is easily manufactured and physically stable.[6]
6. They offer a larger interfacial area for medication partitioning between oil and water than oily solutions do.
7. SEDDS minimize the irritation commonly experienced during prolonged contact between the bulk drug substance and the gut wall by assisting in the wide dispersion of the drug across the stomach and promoting wide distribution of the drug throughout the GI tract.[7]
8. These methods may offer the following benefits: improved oral bioavailability, more stable temporal patterns of drug absorption, targeted drug

delivery to a particular GI tract absorption window, and protection of the drug from the harsh gut environment. The rate and extent of absorption may be improved by these systems, leading to more repeatable blood time profiles for lipophillic medicinal molecules that show dissolution rate limited absorption.[8]

Restrictions on SEDDS

High production costs, poor drug stability and incompatibility, drug leakage and precipitation, and capsule aging are some drawbacks of conventional SEDDS, which are mostly made in liquid form and taken orally in soft or hard gelatin capsules. When liquid SEDDS are incorporated into a solid dose form, it is both attractive and appealing. Recently, researchers have looked into a new drug delivery technique called solid SEDDS (S-SEDDS), which combines the benefits of solid dosage forms and SEDDS. High Solubility and Permeability in

Class I Examples include Propranolol, Metoprolol, Diltiazem, and Verapamil;
Class II: Low Solubility and High Permeability For example, mefenamic acid, ketoconazole, nifedipine, nicardipine, felodipine, and piroxicam
Class III: Solubility is high and permeability is low Examples include enalaprilate, alendronate, captopril, acyclovir, and neomycin B.
Class IV: Low solubility and low permeability for example, flurosemide, tobramycin, and chlorthiazide. The three main parameters that determine oral drug absorption—dissolution, solubility, and intestinal permeability—can be estimated using this drug research tool. The low solubility of BCS Class II and IV medications presents a variety of difficulties for formulation scientists working on oral drug administration.[9]

Self-Emulsifying Drug Delivery Systems

The capacity of self-emulsifying drug delivery systems to increase the bioavailability of medications that are poorly soluble in water has made them popular. Because of this, a lot of medication candidates that exhibit promising pharmacodynamic efficacy never make it to market.[10] Lipid formulations use Systems for Self-Emulsifying Drug Delivery (SEDDS). These formulations are made up of isotropic pharmacological combinations, most often lipids or surfactants.[11-13] With a co-solvent or co-emulsifier that is hydrophilic. Following a small amount of stirring and water dilution, this technology instantly generates an emulsion. The resulting emulsions have droplets that range in size from a few nanometers to many microns. This technique can be used to increase the solubility of any medication in the BCS class. Because SEDDS bypass the dissolving stage, which can slow down the rate at which hydrophobic medications are absorbed, they assist keep the pharmaceuticals soluble in the gastrointestinal system. Particle size and droplet polarity are the two primary parameters that influence the drug release rate in SEDDS. A minimal number of excipients is ideal for the most efficient formulation. The core of SEDDS is excipients.Lipids, surfactants, and co-solvents are the most commonly utilized excipients. Excipients that improve medication solubility are the best options. Lipids are useful for improving the solubility and transportation of lipophilic medications.[14] Large volumes of hydrophobic medicinal compounds can be dissolved by surfactants because they are ampiphilic. Hydrophilic surfactants are commonly used in high concentrations as co-solvents. Self-Micro Emulsifying Drug Delivery Systems (SMEDDS) are created when surfactant and co-surfactant are combined, and their droplet sizes range from 100 to 200 nm.[15] The capacity to create tablets and capsules with good flow ability, cohesive qualities, and content consistency is one

benefit of using SEDDS and SMEDDS. Outstanding product performance, design, and manufacturing capabilities are made possible by this process. Understanding the precise application of SEDDS and SMEDDS on drug deposition as lipid formulations has just lately become clear.

Formultaion consideration of SEDDS

SEDDS considered in the formulation When creating formulations based on lipids, the following factors are thought to be crucial: The solubility of the medicine both in the formulation and after dissolution. The solubilization capacity of the digested formulation and, potentially, the pace of digestion (for formulations that are vulnerable to digestion).

EXCIPIENTS

Oils:

At room temperature, the oily/lipid component is often a medium/long chain saturated, partially unsaturated hydrocarbon or fatty acid ester in liquid, semisolid, or solid form. Mineral oil, vegetable oil, silicon oil, lanolin, refined animal oil, fatty alcohols, fatty acids, and mono-, di-, and tri glycerides are a few examples. Although unmodified edible oils offer the most "natural" foundation for lipid vehicles, their usage in SEDDS is significantly reduced due to their inability to dissolve large quantities of hydrophobic medicines and their relative difficulty in self-emulsifying effectively. On the other hand, hydrolyzed or modified vegetable oils provide physiological and formulative benefits. Since many non-ionic surfactants are authorized for oral administration and their breakdown products mimic the final products of intestinal digestion, these excipients make effective emulsification systems.[16]

Surfactant:

The most commonly advised surfactants are non-ionic ones that have a comparatively high hydrophilic–lipophilic balance (HLB) value. Excipients that are most commonly utilized are polyoxyethylene 20 oleate (Tween 80) and other liquid or solid ethoxylated polyglycolyzed glycerides. The use of natural emulsifiers is advised for SDLF (self-dispersed lipid formulation) and is anticipated to be safer than synthetic ones. Although non-ionic surfactants are known to be less harmful than ionic surface-active chemicals, they have the potential to modify intestinal wall permeability in a somewhat reversible way. Stable SEDDS are formed when the surfactant concentration is between 30% and 60% (w/w). An excessive amount of surfactant might cause gastrointestinal irritation. To provide a good dispersing/self-emulsifying performance, surfactants must have a high HLB and consequently be hydrophilic in order to create o/w droplets immediately and/or disperse the formulation quickly in the aqueous environment. Due to their amphiphilic character, the surface-active agents may typically dissolve and even solubilize rather large quantities of the hydrophobic medication. The latter is crucial for keeping the drug molecules in a soluble state for an extended period of time, which is necessary for efficient absorption, and for preventing precipitation within the GI lumen. When lipid mixtures have larger ratios of surfactant and co-surfactant to oil, self-micro emulsifying formulations (SMEDDS) are created.[17]

Co-solvents:

Co-solvents are employed in SEDDS to dissolve hydrophilic surfactants or hydrophobic drugs in lipid bases in large quantities. Occasionally, these solvents function as co-surfactants in the[18] Systems of microemulsions. Tetrahydrofurfuryl

alcohol polyethylene glycol ether (Glycofurol), propylene glycol, polyethylene glycol, polyoxyethylene, propylene carbonate, and diethylene glycol monoethyl ether (transcutol) are among the co-solvents utilized in SEDDS.

METHODS OF PREPARATION

Solid self-emulsifying drug delivery system

Approaches to preparation Solid self-emulsifying drug delivery systems, or SEDDS, can be solid or liquid. However, since many of the excipients used in SEDDS are not solids at room temperature, SEDDS are typically only available in liquid dosage forms. S-SEDDS have been widely used in recent years because to the benefits of solid dosage forms, which often offer more potent substitutes for traditional liquid SEDDS. In terms of dosage forms, S SEDDS refers to solid dosage forms that have the ability to self-emulsify.S-SEDDS focuses on using various solidification methods, such as melt extrusion, spray drying, adsorption to solid carriers, and nanoparticle technologies, to incorporate liquid or semi-solid SE components into powders or nanoparticles. Typically, these powders or nanoparticles—which are also known as SE nanoparticles14, dry emulsions, or solid dispersions—are processed further into further solid SE dosage forms or, as an alternative, put into capsules (also known as SE capsules). Another type of SE capsule is one that has liquid or semi-solid SEDDS added straight to it without the need of any solidifying agents. Since S-SEDDS are essentially combinations of SEDDS and solid dosage forms, many of its characteristics (such as excipient selection, specificity, and characterisation) are the sum of the equivalent characteristics of SEDDS and solid dosage forms.For example, in addition to evaluating self-emulsification, the characterizations of SE pellets also include surface roughness, friability, and other factors. Other solid SE dosage forms, including SE pellets/tablets, SE microspheres/nanoparticles, and SE suppositories/implants, have recently surfaced. In the 1990s, S-SEDDS were typically in the form of SE capsules, SE solid dispersions, and dry emulsions.

Applications of SEDDS

SEDDS applications the following formulation strategies have been investigated in an effort to maximize bioavailability, achieve sustained release, and prevent biodegradation

Self-emulsifying capsules:

capsules that emulsify themselves: Following the ingestion of capsules containing traditional liquid SE formulations, microemulsion droplets are created and then spread throughout the gastrointestinal tract to reach absorption sites. However, an enhancement in medication absorption cannot be anticipated if the micro emulsion undergoes irreversible phase separation. Sodium dodecyl sulphate was added to the SE Formulation in order to address this issue.Using a modest amount of HPMC (or other polymers) in the formulation, the supersaturatable SEDDS was created with a similar goal in mind: to prevent drug precipitation by creating and preserving a supersaturated state in vivo. Because there is less surfactant in this method, there are less GI side effects. In addition to liquid filling, solid carriers (adsorbents, polymers, etc.) can be added to liquid SE components to load them into capsules in a solid or semisolid state.[19]

Dry emulsions:

Powders that spontaneously emulsify in vivo or when exposed to an aqueous solution are known as dry emulsions. For additional tablet and capsule preparation, dry emulsions may be helpful. Usually, rotary evaporation is used to create dry

emulsion formulations from oil/water (O/W) emulsions that contain a solid carrier (lactose, maltodextrin, etc.) in the aqueous phase.[20]Freeze-drying[21]Or spray drying.[22] When making dry emulsions, the spray drying method is more commonly employed. Tablets and capsules can be further prepared using dry emulsions. Most recently, Dextran 40, a water-soluble solid carrier, has been used to create nimodipine dry emulsions.[22] The most intriguing discovery in this area is the recently created enteric coated dry emulsion formulations, which may be used for the oral administration of protein and peptide medications. These formulations involve lyophilization and include a pH-responsive polymer, a vegetable oil, and a surfactant.[23]

Self-emulsifying Tablets

Tablets that Emulsify Their Own A self-nanoemulsified tablet dosage form of ubiquinone was created by Nazzel et al. (2002). Examining the impact of formulation components on ubi-Quinone release rate and assessing an ideal formulation for self-nano emulsified tablets were the primary goals of this study. Ubiquinone was present in the first self-nanoemulsion system, which was made as a nanoemulsion that was compressed into tablets after being absorbed by granular materials. According to the dissolving profile of the coenzyme Q10 self-Nano emulsified tablet formulation, 80–90% of the medication was released in 45 minutes.[24] The solid self-emulsifying methods for diclofenac delivery were developed by Attama et al. (2003). This solid self-emulsifying system was created with Tween 65 and goat fat. After heating the fatty substance and surfactant until they melted, they were added to the weighted amount of medicine that had dissolved in the melt. The molten mass was then poured into a plastic mold and allowed to cool. Peristalsis will shorten the liquefaction duration, resulting in faster emulsification with higher plasma concentration. These tablets will liquefy at body temperature without agitation and with agitation in the gastrointestinal tract. The dissolution profile varies with different formulation ratios while maintaining the same speed and agitation. These tablets displayed acceptable tablet characteristics together with good release profiles.[25]

Self-emulsifying Pellets

Pellets with self-emulsification Tuleu and his colleagues (2004) conducted a study comparing the bioavailability of a self-emulsifying progesterone formulation in dogs that was administered as pellets and in liquid form. The study compared the liquid form with an aqueous suspension of progesterone. Progesterone capsules containing progesterone dissolved in a self-emulsifying system dissolved over 100% of the drug after 30 minutes and within 5 minutes, according to in vitro dissolution experiments. Half of the dosage was released from the aqueous suspension in 60 minutes. Also, they demonstrated that the same dosage of progesterone dissolved in liquid SES in capsules or suspension of micronized progesterone was compared against pellets given orally to dogs. It states that, in comparison to the progesterone aqueous suspension, the plasma levels of progesterone were higher in SES pellets and SES solution at every time point.[26] A technique for creating self-emulsifying pellets using wet granulation was created by Franceschinis et al. in 2005. The first thing they did was create a binder solution using oil (mono and diglycerides), polysorbate-80, and the model medication nimusulide in varying amounts. Using a granulator to create granules from lactose and microcrystalline cellulose was the second stage. The granules were sprayed with these binder solutions, and the granulator's speed was increased to form pellets. Pellets were able to produce droplets that were noticeably smaller than those of equivalent emulsions.[27] Using self-

emulsifying pellets, Serratoni et al. (2007) demonstrated regulated drug release. Because more medicine absorbed into SES may precipitate when diluted with water, the prepared self-emulsifying system was created by combining oil and surfactant in the solubilized drug at the proper quantities. Lactose monohydrate and microcrystalline cellulose were combined with this SES to create a damp mass. Water was then added to the created wet mass for extrusion-speronization to create pellets. These pellets were coated with hydrophilic polymers, specifically ethyl cellulose, and then a fluid bed coater consisting of an aqueous solution of hydroxyl-propyl-methyl cellulose. Dissolution findings for the uncoated pellets containing methyl or propyl parabens with and without the inclusion of a self-emulsifying system were examined to see whether this formulation may improve the model drug's dissolution.[28] The formulation of self-emulsifying pellets was prepared and characterized by Ahmed Abdalla and Karsten Mader. They separately created three self-emulsifying systems by melting solutol HS 15 and Cithrol GMS (mono and diglycerides), then adding medication, dye, and spin probe. After adding water until a creamy mass was formed, dry MCC was added to the molten lipid blend to create an extrusion-ready material. In order to evaluate the self-emulsification, the dye was added, and an electron spin resonance spectrocopy was used to evaluate the release kinetics and pellet microenvironment during the release process.The dissolution profile revealed that the non-self-emulsifying GMS/MCC pellets completely released the medication in the form of diazepam. It acted for three times as long. Only 55% of the medication was released from GMS/MCC pellets, compared to nearly 90% after an hour. Only until the saturation solubility was achieved could diazepam be released from MCC/GMS pellets.Complete drug release as diazepam from the non-self-emulsifying GMS/MCC pellets was demonstrated by the dissolution profile. Its period of action was three times. Only 55% of the medication was released from GMS/MCC pellets after an hour, compared to over 90% of the substance. The MCC/GMS-based pellets could only release diazepam once the solubility approached saturation.[29] Type 1 pellets had formulation A (a lactose and MCC matrix loaded with SES dispersion) in the inner part and formulation B (an inert matrix containing lactose, MCC, and water) in the outer part, while type 2 pellets had formulation B in the inner core and formulation. Iosio et al. (2008) prepared bi-layered self-emulsifying pellets, SEP formed by coextrusion speronization with two cohesive layers. Two stages were taken to construct an external SEP: first, an oil-surfactant mixture was created, which was then mixed with water to create a self-emulsifying system. This mixture was then loaded into MCC and lactose to create an appropriate extrusion speronization mass for pellets.90% of the model drug vinpocetine was released from type I pellets plus 2% croscarmellose sodium in 30 minutes, type II pellets in 20 minutes, and only 25% of the drug was released from the physical combination after 60 minutes.[30]

Self-emulsifying beads

Beads self-emulsifying Using the solvent evaporation approach, Patil and Paradkar examined loading SES into the microchannels of porous polystyrene beads (PPB) to transform it into a solid form with the least quantity of solidifying excipients. PPB with intricate internal void structures is usually created by copolymerizing divinyl benzene and styrene. They are inert and stable in a broad pH range as well as in harsh temperature and humidity conditions. According to the findings of this study, PPB may be used as carriers for SES solidification, and solid form could only be

obtained at high enough SES to PPB ratios. The loading efficiency and in vitro drug release from SES-loaded PPB were found to be governed by geometrical factors, such as the size of the beads and the pore architecture of PPB.[31]

Self-emulsifying nanoparticles:

The creation of SE nanoparticles has benefited from the use of nanoparticle methodologies. Among these methods is solvent injection. This procedure included melting the medicines, lipid, and surfac tant and injecting them drop by drop into a stirred non-solvent. After that, the resultant SEnanoparticles were filtered out and allowed to dry. This method produced nanoparticles with a high drug loading efficiency of 74% that were around 100 nm in size.[32] Co-loading 5-fluorouracil (5-FU) and antisense EGFR (epidermal growth factor receptor) plasmids into biodegradable PLGA/O CMC nanoparticles was accomplished using a second process called sonication emulsion–diffusion–evaporation. In order to administer paclitaxel (PTX), Trickler et al. more recently created a new nanoparticle drug delivery method using glycerylmonooleate (GMO) and chitosan. These chitosan/GMO nanoparticles were made using multiple emulsion (o/w/o) solvent evaporation techniques, and they had bioadhesive qualities and enhanced cellular attachment. Nearly 100% loading of PTX was caused by the SE feature of GMO, which improved PTX's solubility. These benefits reduce the negative side effects linked to medications like PTX by enabling the use of lower dosages of the medicine to establish an effective therapeutic window.[33]

Self-emulsifying capsules

Capsules that emulsify themselves A microemulsion droplet develops and then spreads along the GI tract to reach absorption sites following the intake of capsules containing traditional liquid SE formulations. However, an enhancement in medication absorption cannot be anticipated if the microemulsion undergoes irreversible phase separation. Sodium dodecyl sulfate was used into the SE formulation to address this issue.[34] Using a modest amount of HPMC (or other polymers) in the formulation, the supersaturable SEDDS was created with a similar goal in mind: to prevent drug precipitation by creating and preserving a supersaturated state in vivo. Because there is less surfactant in this method, there are less GI side effects.[35-36] In addition to liquid filling, solid carriers (adsorbents, polymers, etc.) can be added to liquid SE components to load them into capsules in a solid or semisolid form. For instance, a solid PEG matrix may be used. The drug's solubility and the process of self-micro emulsification upon mixing with water were unaffected by the presence of solid PEG.[37-38] When compared to the previously employed parenteral approach, oral administration of SE capsules has been demonstrated to improve patient compliance. For example, the sole clinically accessible method of administering low molecular weight heparin (LMWH), which is used to treat venous thromboembolism, was parenteral. Therefore, the formulation of oral LMWH treatment in hard capsules was studied. After dispersing LMWH in SMEDDS, the mixture was consolidated into powders using three different types of adsorbents: silicon dioxide (Sylysia 320), magnesium aluminum silicate (Neusilin TM US2), and micro porous calcium silicate (Florite TM RE). These solids were eventually put into rigid capsules.[39] In a different investigation, these adsorbents were also used to create SE tablets of gentamicin, which were only administered as topical or injectable dose forms in clinical settings.[40]

Self-emulsifying Microspheres

Microspheres that emulsify themselves Solid self-sustaining release microspheres were created by You et al. in 2005 utilizing the quasi-emulsion solvent diffusion method for spherical crystallization. The ratio of hydroxypropyl methylcellulose acetate succinate to Aerosil 200 in the formulation might regulate the release behavior of zedoary turmeric oil. Following oral administration of such microspheres to rabbits, plasma concentration time profiles were obtained, and the bioavailability was 135.6 percent in comparison to conventional liquid SEDDS.[41]

Self-emulsifying suppositories

Some investigators proved that S-SEDDS could increase not only GI adsorption but also rectal/vaginal adsorption[42] Using either vaginal or rectal SE suppositories, glycyrrhizin—which, when taken orally, seldom ever reaches therapeutic plasma concentrations—can produce enough therapeutic levels for chronic hepatic disorders. Glycyrrhizin and a combination of a C6–C18 fatty acid macrogol ester and a C6–C18 fatty acid glycerol ester were added in the formulation.[43]

Self-emulsifying implants:

S-SEDDS's usefulness and use have been substantially expanded by research into SE implants. For instance, the chemotherapy drug 1, 3-bis (2-chloroethyl)-1-nitrosourea (carmustine, BCNU) is used to treat malignant brain tumors. Its brief half-life, however, limited its efficacy. Tributyrin, Cremophor RH 40 (polyoxyl 40 hydrogenated castor oil), and Labrafil 1944 (polyglycolyzed glyceride) were added to SES to increase its stability as compared to that released by polyd,l-lactide-co glycolide (PLGA) wafer implants. The self-emulsified BCNU was then compression-molded into wafers with a smooth, flat surface. Finally, compared to 45 minutes of intact BCNU, SES extended the in vitro half-life of BCNU to 130 minutes.BCNU's in vitro release from SE PLGA wafers was extended for up to seven days. Compared to wafers without SES, these wafers exhibited greater in vitro anticancer activity and were less susceptible to hydrolysis.[44]

METHODS OF PREPARATION

Solid self-emulsifying drug delivery system

Approaches to preparation Solid self-emulsifying drug delivery systems, or SEDDS, can be solid or liquid. However, since many of the excipients used in SEDDS are not solids at room temperature, SEDDS are often only available in liquid dosage forms. S-SEDDS have been widely used in recent years because to the benefits of solid dosage forms, which often offer more potent substitutes for traditional liquid SEDDS. In terms of dosage forms, S SEDDS refers to solid dosage forms that have the ability to self-emulsify. S-SEDDS concentrate on incorporating liquid or semi-solid SE components into powders or nanoparticles using various solidification methods, such as melt extrusion, spray drying, adsorption to solid carriers, and nanoparticle technology. These powders or nanoparticles are known as SE nanoparticles.[45] /dry emulsions/solid dispersions, are often packed into capsules (i.e., SE capsules) or subsequently processed into different solid SE dosage forms. SE capsules are also those that are filled directly with liquid or semi-solid SEDDS without the need of any solidifying excipients. Many of the qualities of S-SEDDS, such as excipient selection, specificity, and characterisation, are the total of the equivalent properties of both SEDDS and solid dosage forms since S-SEDDS are, in part, mixtures of SEDDS and solid dosage forms. For example, in addition to evaluating self-emulsification, the characterizations of SE pellets also include surface roughness, friability, and other factors.Other solid

SE dosage forms, including SE pellets/tablets, SE microspheres/nanoparticles, and SE suppositories/implants, have recently surfaced. In the 1990s, S-SEDDS were typically in the form of SE capsules, SE solid dispersions, and dry emulsions.

Formulation Techniques Of S-Sedds

Transforming liquid/semisolid SEDDS to S-SEDDS

This has been developed for the controlled administration of insoluble pharmacological compounds or peptides along with the advancements in capsule technology. This system is a liquid SE formulation system that operates on osmotic principles. The medication formulation is pumped through an opening in the hard or soft capsule by an osmotic layer that swells upon coming into contact with water.[46] The compatibility of the excipients with the capsule shell Is a key factor in capsule filling. Cole et al. identified the liquid/semisolid lipophilic vehicles that work with hard capsules. [47-48] Simple manufacture, high drug loading (up to 50% (w/w)), and appropriateness for low-dose, very powerful medications are the benefits of capsule filling.[49]

Spray dried

Spray-dried This method basically entails creating a formulation by combining lipids, solid carriers, drugs, and surfactants, then solubilizing the mixture before spray drying it. The liquid composition that has been dissolved is then atomized to create a droplet spray. The droplets are placed in a drying chamber with regulated airflow and temperature where the volatile phase (such as the water in an emulsion) evaporates to generate dry particles. These particles can be further processed to create capsules or tablets. The drying properties of the product and powder specifications are taken into consideration while choosing the atomizer, temperature, appropriate airflow pattern, and drying chamber design.

Melt extrusion/extrusion spheronization

Melt extrusion is a solvent-free method that enables homogeneous content and high drug loading (60%) 15. Extrusion is the process of pushing a raw material having plastic qualities through a die under carefully regulated pressure, temperature, and product flow conditions to create a product with a consistent shape and density.[50] The approximate size of the produced spheroids will depend on the size of the extruder aperture. The pharmaceutical industry frequently uses the extrusion–spheronization technique to create spheroids (pellets) of uniform size. The following actions are necessary for the extrusion-spheronization process: Extrusion into a spaghetti-like extrudate, spheronization from the extrudate to spheroids of uniform size, drying, sifting to obtain the required size distribution, and coating (optional) are the steps involved in dry mixing the active components and excipients to create a homogenous powder.The extrusion force, size spread, disintegration time, and surface roughness of pellets were significantly impacted by the relative amounts of SES and water in the wet masses that contained lactose, water, MCC, and SES (Polysorbate 80 and mono-/di-glycerides). According to studies, 42% of the dry pellet weight is the highest amount of this SES that can be solidified by extrusion spheronization.[51]In general, the disintegration time increases with increasing water level.[52] An extrusion capillary can be used to test the rheological characteristics of wet bulk. It has been demonstrated that SES with wet mass that exhibits a broad range of rheological properties may be treated; nevertheless, extrusion-spheronization cannot give comprehensive characterisation using a single rheological measure.[53] Bi-layered cohesive SE

pellets containing progesterone and diazepam were created by using extrusion spheronization.

CONCLUSION

Self-emulsifying pellets represent a significant advancement in oral drug delivery systems, particularly for drugs with limited solubility and bioavailability. By combining the benefits of self-emulsifying drug delivery systems (SEDDS) with the advantages of multiparticulate dosage forms, these formulations offer improved stability, enhanced drug release, and better patient compliance. The selection of appropriate oils, surfactants, co-surfactants, and solid carriers is critical to achieving an optimal formulation. Techniques such as extrusion–spheronization enable the production of uniform, spherical pellets with desirable mechanical and dissolution characteristics. Moreover, the application of quality-by-design (QbD) and statistical optimization methods can significantly streamline the development process and ensure product consistency. While challenges remain in terms of large-scale manufacturing and long-term stability, current research demonstrates promising outcomes, especially in the delivery of drugs like Venlafaxine Hydrochloride. Future investigations focusing on in vivo studies, scalability, and regulatory perspectives will further establish self-emulsifying pellets as a versatile and efficient platform in the pharmaceutical industry.

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HOW TO CITE: Akshay Jadhav*, Dr. Ravi Wanare, Aniket Kadam, Rehan Beniwale, Ankita Tayade, Advances in Self-Emulsifying Drug Delivery Systems: Focus on Pellet-Based Formulations, Int. J. of Pharm. Sci., 2025, Vol 3, Issue 4, 2033-2046. https://doi.org/10.5281/zenodo.15231553